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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/053.669	01/24/2002	Ibert C. Wells	N1427-005	1066

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EXAMINER	
SZPERKA, MICHAEL EDWARD	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 08/04/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/053,669	WELLS, IBERT C.	
	Examiner	Art Unit	
	Michael Szperka	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 June 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,9,28,30 and 32-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,9,28,30 and 32-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/14/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's response and amendments received June 1 are acknowledged.

Claims 2-8, 10-27, 29, and 31 have been canceled.
Claims 1 and 9 have been amended.

Claims 1, 9, 28, 30, and 32-34 are under examination as they read on monoclonal antibodies that bind the tetrapeptide of SEQ ID NO:2.

Information Disclosure Statement

2. Applicant's IDS received November 14, 2005 is acknowledged and has been considered.

Declaration

3. The declaration of Ibert C. Wells under 37 CFR 1.132 is acknowledged and will be discussed with applicant's other arguments as they pertain to the rejection of record.

Specification

4. Applicant's amendment to the title of the invention to include antibodies, the subject matter claimed in the instant application is acknowledged.

The objection to the abstract is because it only contains generic statements about the methods disclosed in the specification and does not discuss antibodies, the subject of the claims currently under examination, is maintained. Amending the abstract to include the instant claimed subject matter is appropriate. Applicant has not amended the abstract as part of the reply received June 1, 2006 and has not presented arguments as to why such changes are unnecessary.

Claim Rejections - 35 USC § 102

5. The rejection of claims 1-6, 28, and 30 under 35 U.S.C. 102(b) as being anticipated by Couraud et al. (J. Neurochemistry, 1987, 49:1708-1718, of record, see entire document) has been withdrawn. Specifically, on June 1, 2006 applicant has amended independent claim 1 to recite that the claimed monoclonal antibody specifically binds the tetrapeptide of SEQ ID NO:2. The antibodies of Couraud et al. are specifically taught as not binding this sequence, and as such the rejection has been withdrawn.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1, 9, 28, 30, and 32-34 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention for the reasons of record.

The office action mailed December 1, 2005 states that:

> Applicant's arguments filed September 1, 2005 have been fully considered but they are not persuasive. Applicant has argued that only routine experimentation would be required to generate an antibody that binds to a peptide consisting of SEQ ID NO:2. SEQ ID NO:2 is a tetrapeptide that is completely contained within the larger pentapeptide of SEQ ID NO:1. SEQ ID NO:4 is degenerate pentapeptide that contains SEQ ID NO:1 and the sequence FVGLM. Applicant argues that it was recognized in the art that epitopes are often comprised of only 4 or 5 amino acids, and that only routine screening would be required to find an antibody that had the ability to bind to a tetrapeptide consisting of SEQ ID NO:2. The examiner agrees that antibodies may be able to bind a linear peptide epitope that consists only of four amino acids, and as such tetrapeptides can be *antigenic*. However, it is not routine in the art to make antibodies using such a short peptide sequence since as taught by Harlow et al. (of record), the smallest synthetic peptide sequence that consistently elicits an antibody response (and hence is *immunogenic*) is 6 amino acids in length, with approximately 10 amino acids being preferred. As such, it is routine to raise antibodies against a larger immunogenic polypeptide and then map the antibody binding to a smaller antigenic peptide sequence. As has been stated in the rejections of record, Couraud et al. (J Neurochem, 1987, 49:1708-1719, of record, see entire document) performed standard, art recognized procedures described by Harlow et al. in generating their antibodies. Specifically, they teach polyclonal and monoclonal antibodies that were generated using the 11 amino acid neuropeptide substance P (SP), and they mapped the binding of these reagents to smaller polypeptide sequences. Their data indicated that while antibodies that bind a pentapeptide consisting of SEQ ID NO:1 were readily observed (the polyclonal serum and 5 out of 5 distinct monoclonal antibodies), no reactivity was observed to the tetrapeptide

consisting of SEQ ID NO:2. The lack of binding in the polyclonal serum is particularly noteworthy, since it indicates that antibodies with the requisite binding specificity are not readily generated.

Given that the application does not disclose a working example of the claimed antibodies that are raised against such a small polypeptide sequence, that antibodies that bind some but not all SP fragments as taught by Couraud et al. were generated using standard, art recognized techniques, that while it is known that antibodies can bind small linear peptides, such as a peptide consisting of 4 amino acids, it is not routine to generate antibodies using such small sequences as an immunogen as taught by Harlow et al., and since the specification does not indicate that anything other than standard art recognized procedures are required to make an antibody that binds a tetrapeptide consisting of SEQ ID NO:2, it does not appear that a skilled artisan would be able to make and use the full breadth of applicant's claimed invention, especially in the absence of evidence to the contrary. Therefore the rejection of record is maintained.

Applicant's arguments and the declaration of Ibert C. Wells filed June 1, 2006 have been fully considered but they are not persuasive. Applicant argues on two grounds. First is a repetition of arguments of record that no more than routine experimentation is required to make the claimed antibodies. The second argument is that the teachings of Couraud et al. do not demonstrate a lack of enablement for the claimed antibodies because the structure of immunogen used by Couraud et al. in generating anti-substance P antibodies precludes the generation of antibodies that comprise the recited binding specificities. Applicant points to the declaration of Ibert C. Wells to support both arguments.

Native SP peptide is amidated at its carboxyl terminal. The declaration states that the immunogen of Couraud et al. was made by first removing the amide group from the carboxyl terminal of SP and then coupling the carboxyl terminal to BSA, and points to pages 1709 and 1717 of Couraud for support. The declaration further states that such a construct would not allow for interaction between antibody producing cells and an amidated carboxyl terminus of SP. Applicant argues that this is why Couraud et al. failed to observe antibody binding to the SP tetrapeptide of SEQ ID NO:2. Applicant also argues that the SP fragments used in epitope mapping did not comprise an amidated carboxyl group, and points to page 1712 of Couraud for support.

Couraud et al. teach "[O]ur five mouse mAbs are directed against the C-terminal part of SP. This was expected from the structure of the immunogen in which SP is conjugated to BSA through the basic residues in its N-terminal moiety." (See the top of the right column of page 1717). Further, later work by the same laboratory in characterizing one of the five monoclonals disclosed by Couraud et al. states "Immunization as well as monoclonal antibody selection procedures have been already

described in detail. (citation to Couraud et al.) In brief, immunogen was obtained by coupling SP to bovine serum albumin via its N-terminal (αNH_2 of Arg^1), which allows selection of antibodies directed at the C-terminal of the peptide." (See the first two sentences of the Materials and Methods subsection *mAbs Production and Selection* of page 68 of Dery et al., of record on the IDS received 3/7/05). This later work further states that the five residues Phe-Phe-Gly-Leu-Met-NH_2 are necessary for binding to the SP31 mAb (see the Conclusion section on page 73 of Dery et al.). Note that SP31 is one of the five monoclonal antibodies disclosed by Couraud et al. Therefore, the structure of the immunogen used by Couraud et al. is not the structure described by Ibert C. Wells in his declaration. It appears that Ibert C. Wells has misinterpreted the teachings of Couraud et al., and as such the declaration is not persuasive because it is based upon a faulty premise.

Applicant also argues that "[the declaration of Ibert C. Wells] clarifies that Couraud et al. evaluate the cross-reactivity of their five selected monoclonal anti-SP antibodies and polyclonal serum using SP fragments that do not include an amidated carboxyl group (See page 1712)." Support for this statement cannot be located by the examiner either in the declaration of Ibert C. Wells or on page 1712 of Couraud et al. As stated previously, native SP is amidated at its carboxyl terminal, and as such N-terminal truncations of SP comprise an amidated carboxyl terminal. Given the above discussion concerning the structure of the immunogen used by Couraud et al., it is clear that the amidated carboxyl terminus of SP was available for interaction with antibody producing cells, contrary to applicant's arguments. As such, the failure of Couraud et al. to observe antibody binding to the tetrapeptide when antibody binding to the recited pentapeptides were readily apparent indicates that antibodies of the recited binding specificity are not generated using standard art techniques for antibody production. The specification does not teach antibody production methods that differ from standard, prior art techniques, and as such a skilled artisan would not reasonably expect to be able to make the recited antibodies using the teachings of the instant specification.

The rejection of record is maintained.

8. No claims are allowable.

9. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Szperka whose telephone number is 571-272-2934. The examiner can normally be reached on M-F 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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July 25, 2006

7/27/06
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PRIMARY EXAMINER